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The Gene Expression Profile and DNA Methylation Pattern of CDH1 and DNMT1 Genes in Acute Promyelocytic Leukemia (APL)

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Abstract

Background: DNA methylation is an epigenetic modification that has the ability to alter gene expression and function. These epigenetic changes have been associated with the development of cancer. Previous research has found that DNA methylation patterns can predict disease prognosis for patients with Acute Promyelocytic Leukemia (APL). The role of DNMT1 and CDH1 in regulating the extension of cells are studied in this study.
Methods: DNA was extracted from peripheral blood samples of APL patients and treated with bisulfite. DNMT1 and CDH1 gene promoter methylation was subsequently analyzed using methylation-specific PCR (MSP). Real-time PCR was used to measure the expression level of DNMT1 and CDH1 genes.
Results: Partial methylation of the CDH1 gene promoter was detected in 20% of APL patients and an unmethylated status was detected in 80% of patient samples. Additionally, an unmethylated status in the DNMT1 gene promoter was detected in 100% of APL patient samples.
Conclusions: Our study found the CDH1 gene promoter to be unmethylated in almost all APL patients, while the DNMT1 promoter was unmethylated in all APL patients. Furthermore, we observed an increase in both CDH1 and DNMT1 gene expression in APL patients compared to healthy controls. These findings suggest that DNMT1 may not have a specific role in inhibiting CDH1 gene expression in APL. Applying higher resolution techniques would help to better uncover the DNA methylation patterns in patients with APL. Further research is required to determine the role of DNA methylation and CDH1 and DNMT1 gene expression in APL.

Keywords: Acute Promyelocytic Leukemia, CDH1, DNMT, Promoter Methylation.

Introduction

Acute myeloid leukemia (AML) is a hematopoietic malignancy in which incompletely differentiated hematopoietic progenitor cells accumulate in the bone marrow and blood, interfering with normal hematopoiesis. Research has shown that the accumulation of mutations and epigenetic modifications are key features in the AML genome. Both of these alterations often occur prior to the development of leukemia and persist in residual disease following therapeutic intervention. Thus, targeting the AML epigenome may help cure the residual disease and prevent cancer recurrence (1). The treatment interventions for AML have remained relatively unchanged over the past few decades, however there have been some improvements in the survival outcomes for younger patients (2). In spite of these improvements, AML treatment interventions are unsuccessful for about 60% of young patients (3). In patients over the age of 60, in which there is an increased frequency of

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